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### REMARKS

Claims 59, 62, 65-94, and 124 are pending.
Claims 59, 89-94, and 124 are currently amended.
Claims 1-58, 60-67, 69, 70, 77, 95-123, and 125 are canceled.

Claims 59, 68, 71-76, 78-94, and 124 would be all of the claims remaining in the present application if the present amendment is entered.

## Discussion of Claim Amendment

Claim 59 is currently amended to delete "neuropathic" and insert instead "chronic" and to incorporate the limitation of dependant claim 66, which has been canceled. Claim 59 is also currently amended to move the definitions of  $R_2$  and  $R_3$  closer to the end of the claim. Claim 59 is also currently amended to incorporate the limitations of any one of dependent claims 68, 71-76, and 78-88. As currently amended, claim 59 relates to a method of treating chronic pain wherein the chronic pain is associated with arthritis. Claims 68, 71-76, and 78-88 depend from claim 59. Claims 89-94 and 124 are currently amended to independent form.

## Claim Rejections - 35 U.S.C. § 112

In the Office Action, claims 59, 62, 65-94, and 124 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It was stated in the Office Action that omission of the element "chronic pain" in the claims is deemed to raise a new matter issue. Further, the proviso in claim 59 is deemed to insert new matter and the specification as originally filed was alleged to not provide adequate support for the subgenus of compounds now claimed as a result of the proviso.

Applicants respectfully traverse the rejection because claims 62, 65-67, 69, 70, and 77 are canceled, rendering the rejection of claims 62, 65-67, 69, 70, and 77 moot, and because claim 59 has been amended to restore the element chronic pain and to delete the proviso, claims 68, 71-76, and 78-88 depend from claim 59, and claims 89-94 and 124 are now independent.

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In the Office Action, claims 59-87 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 59 recites " $R_2$  and  $R_3$ " and it is stated in the Office Action that there is insufficient antecedent basis for this limitation since there is not  $R_2$  and  $R_3$  described in the structural formula (i)B, "W," and  $R_1$ . Applicants traverse the rejection because claims 60-67, 69, 70, and 77 are canceled, rendering the rejection of claims 60-67, 69, 70, and 77 moot, and because the definitions of  $R_2$  and  $R_3$  have been moved in claim 59 and now  $R_2$  and  $R_3$  each have antecedent basis in claims 59, 68, 71-76, and 78-87.

# Claim Rejections - 35 U.S.C. § 102

In the Office Action, claims 59, 62, 65, 66, 69, and 70 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Connor et al. (EP 0 316 630 A). Applicants traverse the rejection because claims 62, 65, 66, 69, and 70 are canceled, rendering rejection of claims 62, 65, 66, 69, and 70 moot, and because claim 59 incorporates the limitations of any one of dependent claims 68, 71-76, and 78-88.

In the Office Action, claims 59, 62, 65, and 70 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fujimura et al. (Hydcoxayic acid derivatives, Chemical Abstracts vol. 70, no. 3, January 20, 1966, or JP 42 024578 A or JP 42019583 B4, 1967). Applicants traverse the rejection because claims 62, 65, and 70 are canceled, rendering rejection of claims 62, 65, and 70 moot, and because claim 59 incorporates the limitations of any one of dependent claims 66, 68, 71-76, and 78-88.

In the Office Action, claims 59, 62, 65, and 69 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Morkhort, of record). Applicants traverse the rejection because claims 62, 65, and 69 are canceled, rendering rejection of claims 62, 65, and 69 moot, and because claim 59 incorporates the limitations of any one of dependent claims 66, 68, 71-76, and 78-88.

In the Office Action, claims 59, 62, 65, 66, 69, and 77 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hirano Hiroshi et al. (JP 42019583 B4, 1967). Applicants traverse the rejection because claims 62, 65, 66, 69, and 77 are canceled, rendering rejection of claims 62, 65, 66, 69, and 77 moot, and because claim 59 incorporates the limitations of any one of dependent claims 68, 71-76, and 78-88.

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# Claim Rejections - 35 U.S.C. § 103

In the Office Action, claims 59-94 and 124 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Barrett et al. (WO 99/01421) in view of Walker et al. (British Journal of Clinical Pharmacology, 1993;36(5):417-425), and Ma et al. (Brain Research, 1991;566(1-2):95-102) for the reasons of record in the previous Office Action mailed November 17, 2004. It was stated in the Office Action that Barrett et al. disclose compounds that read on the instant active compounds or are structurally substantially similar to the instant compounds that are useful in pharmaceutical compositions and methods for treating inflammation. It was further alleged in the Office Action that Ma et al. teach that pain (e.g., neuropathic pain) is known to be associated with MEK (see Abstract in particular) and Walker et al. teach that pain is well-known to be associated with inflammation (see Abstract in particular).

Applicants traverse the rejection because:

- claims 60-67, 69, 70, and 77 are canceled, rendering rejection of claims
   60-67, 69, 70, 77 moot, and
- claims 59, 68, 71-76, 78-94, and 124 are patentable because Ma et al. is
  an irrelevant reference since the reference does not relate to the instant
  MEK enzyme, and thus (i) the references when combined do not teach
  or suggest the claim limitation of pain being associated with MEK and (ii)
  there is no suggestion or motivation in Barrett et al. in view of Walker et
  al. and Ma et al. to treat chronic pain associated with arthritis with the
  instant MEK inhibitors.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicants' disclosure. (MPEP § 2142)

The instant MEK kinases clearly are not referenced in Ma et al. The "MEK" mentioned by Ma et al. is an opioid peptide, Met-enkephalin (see

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Abstract). Met-enkephalin is comprised of  $\underline{4}$  amino acid residues and has a molecular formula of  $C_{27}H_{35}N_5O_7S$ , a Chemical Abstracts Registry number [58569-55-4], and the following structure:

$$\begin{array}{c|c} & & & & \\ & &$$

In contrast, the "MEK" referenced in the instant specification are kinase enzymes comprised of over 200 amino acid residues (see page 13, lines 15-18). The specification clearly teaches enough about the instant MEK kinases for the Skilled Artisan to know that the instant MEK kinases are not the same as the Met-enkephalin referenced in Ma et al.

Ma et al. is thus not relevant to the present rejection and should be removed therefrom.

With the Ma et al. reference removed from the present rejection, (i) Barrett et al. in view of Walker et al. and Ma et al. do not teach or suggest the claim limitation of pain being associated with MEK and (ii) Barrett et al. in view of Walker et al. and Ma et al. does not suggest or motivate the Skilled Artisan to treat chronic pain associated with arthritis with the instant MEK inhibitors. Accordingly, Applicants believe that claims 59, 68, 71-76, 78-94, and 124 are not obvious and are patentable under 35 U.S.C. § 103(a) over Barrett et al. in view of Walker et al. and Ma et al.

### Double Patenting

Claims 59, 62, 68-94, and 124 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 24, 31, and 33 of U.S. Patent No. 6,310,060. Applicants traverse the rejection because claims 62, 69, 70, and 77 are canceled, rendering rejection of claims 62, 69, 70, and 77 moot, and because claim 59 incorporates the limitation of claim 66.

Claims 59, 62, 68-94, and 124 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 34, 35,

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41, and 43 of U.S. Patent No. 6,506,798. Applicants traverse the rejection because claims 62, 69, 70, and 77 are canceled, rendering rejection of claims 62, 69, 70, and 77 moot, and because claim 59 incorporates the limitation of claim 66.

### Conclusion

In view of the above amendments and remarks, Applicants believe that the rejections of claims 59, 62, 65-94, and 124 are overcome. Applicants request reconsideration of claims 59, 68, 71-76, 78-94, and 124.

Respectfully submitted,

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